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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.                                  | CONFIRMATION NO.                          |
|--|-------------|----------------------|--|---|
| 10/519,983   | 01/04/2005  | Yasuhiro Kajihara    | TAM-051  | 3218                                      |
| <div>20374      7590      12/28/2007</div> <div>KUBOVCIK &amp; KUBOVCIK</div> <div>SUITE 710</div> <div>900 17TH STREET NW</div> <div>WASHINGTON, DC 20006</div> |             |                      |  |   |
|  |             |                      | <div>EXAMINER</div> <div>HEARD, THOMAS SWEENEY</div> |   |
|  |             |                      | <div>ART UNIT</div> <div>1654</div>                  | <div>PAPER NUMBER</div>                   |
|  |             |                      | <div>MAIL DATE</div> <div>12/28/2007</div>           | <div>DELIVERY MODE</div> <div>PAPER</div> |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/519,983

Applicant(s)

KAJIHARA, YASUHIRO

Examiner

Thomas S. Heard

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 07 November 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-12, 15 and 17-21 is/are pending in the application.
- 4a) Of the above claim(s) 15 and 17-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

The Applicants Amendments to the claims received on 11/07/2007 is acknowledged. The text of those sections of Title 35 U.S. Code not included in the action can be found in the prior office action. Rejections or objections not addressed in this office action with respect to the previous office action mailed 9/4/2007 are hereby withdrawn.

Claim(s) 1-12, 15, 17-21 are pending. Applicants have not amended any claims. Claims 15 and 17-21 are withdrawn. Claims 1-12 are hereby examined on the merits.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-12 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al, US Pub No. 2003/0229013 and Toshiyuki et al, Japanese Patent Application No: 10-082882, Applicant's IDS.

The instantly claimed invention is drawn to a process of synthesizing a glycosylated peptide through the use of Solid Phase Chemical Synthesis employing Fmoc protected amino acids and with an Asp amino acid that is coupled to a sugar.

Wu, et al discloses solid phase chemical synthesis employing the common coupling reagents DCC, HOBt-H<sub>2</sub>O, and DIPCDI and resins, such as Wang resin, where the peptide is linked at the C-terminal (Carboxyl) end, see paragraphs [0023] through [0042] for reagents and resins. The synthesis is by coupling the peptide to a resin (Wang) and followed by deprotecting the Fmoc-protected amino-terminus of the peptide and coupling a new Fmoc protected amino protected amino acid to the growing peptide chain. The Fmoc protective reagent used for protecting the amino acids is fat soluble. Wu, et al, does not teach the coupling of an Fmoc protected amino acid that has a sugar residue covalently coupled to the amino acid.

Toshiyuki teaches an Fmoc protected sugar-linked asparagine that is coupled to Fmoc and is used to incorporate a glycosylated amino acid into the synthesis process, see abstract. Toshiyuki et al teaches that the sugar portion of the sugar-linked Asp residues may be a monosaccharide or a sugar chain, readable on having 6 to 9 sugar residues. Toshiyuki et al finally teaches that the hydroxyl residues on the sugar chain may be deprotected, see schemes throughout the entire short application.

The difference between what is instantly claimed and what is taught in the prior art is that the instantly claimed invention incorporates Toshiyuki's Fmoc protected sugar-linked Asp residue. It would have been obvious at the time of the instantly claimed invention to incorporate Fmoc protected sugar-linked Asp residues into the well known Merrifield solid phase peptide synthesis in order to make a glycosylated peptide. One would have been motivated to do so given Toshiyuki's teaching that Fmoc protected sugar-linked Asp residues are compatible with peptide synthesis. One would have had a reasonable expectation of success given Toshiyuki's teaching that sugar-linked Asp residues can be used in peptide synthesis and that the methodology of solid phase synthesis is so well known that one of ordinary skill in the art would be able to adapt the coupling steps beyond Toshiyuki's teaching to incorporate numerous and different sugar residues beyond those instantly claimed. Given the teaching of the references, therefore, it would have been prima facie obvious at the time of the invention to combine the teaching of Wu and Toshiyuki to arrive at the instantly claimed invention.

Applicants arguments have been carefully considered but are not found to be persuasive. Applicants have argued:

First, the Office has not shown where each of the steps recited in claims 1-12 of the present application are disclosed in Wu, alone or as modified by Toshiyuki.

Second, obviousness under 35 U.S.C. § 103(a) requires consideration of the prior art as a whole. The Office has failed to consider the prior art as a whole. Applicant respectfully submits that when the prior art as a whole relating to the preparation of glycopeptides having asparagine-linked oligosaccharides is considered, the Office has not properly supported a case of prima facie obviousness of the process for preparing a glycopeptide having at least one asparagine-linked oligosaccharide as recited in the claims of the present application.

The present application on pages 3-5 describes that the solid- phase synthesis process developed by Merrifield (referred to by the Office in the 35 U.S.C. § 103(a) rejection) is presently in wide use for the preparation of peptides, including glycopeptides. However, such process has the problem of insufficient amounts of oligosaccharides to be linked with the asparagine residue and the possibility that the trifluoroacetic acid treatment for cutting off the peptide chain from the solid phase will cut off sialic acid from the glycopeptide prepared.

Regarding the first argument that the Office has not shown where each of the steps in Claims 1-12 are disclosed in Wu, alone, or a modified by Toshiyuki. The rejection was made under 35 U.S.C. 103(a) which does not require every step to be disclosed in a single reference. Such single disclosures are usually under 35 U.S.C. 102(b). One skilled in the art would readily envision the instant invention by a combination of references and this is evident from the rejection. Regarding the argument that the Office has not considered the art as a whole, is deemed incorrect. The chemistries between solid phase and liquid phase are so similar that one of ordinary skill in the art would readily envision the steps needed to adapt the synthesis to either the liquid phase or solid phase synthesis. The same protected amino acids are used in both and one of ordinary skill in the art would know how to adapt to both liquid and solid phase synthesis.

Applicants further argue:

Wu discloses solid phase chemical synthesis but discloses nothing concerning oligosaccharides. Toshiyuki, on the other hand, discloses nothing concerning solid phase chemical synthesis. Example 4 of Toshiyuki, disclosing preparation of a glycopeptide, does not use a solid carrier (resin). Toshiyuki discloses liquid phase chemical synthesis.

When the disparate disclosures of Wu and Toshiyuki are considered in light of the problems in the prior art for preparing glycopeptides in reasonable amounts and of introducing sialic acid or derivatives thereof into oligosaccharides using solid phase

synthesis, a person of ordinary skill in the art could not have reasonably predicted that the proposed modification of the solid phase chemical synthesis process of Wu would be successful in preparing acceptable amounts of glycopeptides having at least one asparagine-linked oligosaccharide.

Regarding the issue of obviousness, it is noted that the IPER (International Preliminary Examination Report) of the present application found that the process set forth in claims 1-12 is unique in the discovery that sugar chain asparagine can be used in the solid phase synthesis of a peptide without protecting hydroxyl groups. Applicant submits that the reasoning of the IPER is applicable to the propriety of the 35 U.S.C. § 103(a) rejection in the present Action.

As stated in the arguments supra, liquid and solid phase chemistries use the same protected amino acids and one of ordinary skill in the art can modify and optimize the conditions to synthesize the great yield that is possible for each methodologies.

Because of the similarities between the two, one not only motivated to use modified amino acids in the synthesis, one would have been motivated to optimize the conditions to allow compatible steps to assure a high yield of the desired product, much the same manner that is done for both non-glycosylated peptides. Finally, regarding the IPER report and obviousness rejection made by the Office, on the international level, all written opinions are nonbinding and a patent does not issue; what does issue is an international preliminary examination report (IPER), which is nonbinding on the Elected States. See M.P.E.P. § 1878.01, Item V. However, it is of note that Claims 1-21 were found to have a few Y references regarding the instant invention. Therefore, the rejection as made supra is maintained.

### **Conclusion**

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

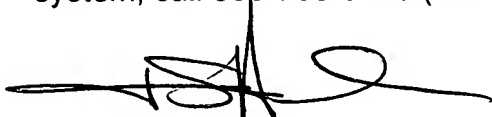
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Thomas S. Heard** whose telephone number is **(571) 272-2064**. The examiner can normally be reached on 9:00 a.m. to 6:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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